Remarks

A. Status of the Claims

Claims 1, 4, 13, 14, 15, 18, 24, 25, 39, 40-42, 44, 46, and 48 are revised to place the claims into a more typical format for U.S. prosecution. Claim 1 is further revised to include additional elements, non-limiting support for which can be found in the original claims and in the specification (*e.g.*, page 9, lines 17-19; page 10, lines 7-9; page 12, lines 18-19, 24, and 31; page 13, line 32, to page 14, line 14).

Claims 2-3, 5-7, 11-12, 16, 20-21, 29-38, 43, 45, 47, and 52-62 are cancelled.

Therefore, claims 1, 4, 8-10, 13-15, 17-19, 22-28, 39-42, 44, 46, and 48-51 are pending.

B. Indefiniteness Rejection

The indefiniteness rejection to claim 25 is moot in view of the removal to the reference of a trademark from this claim. Applicant requests that this rejection be withdrawn.

C. Obviousness Rejection

Claims 1-28 and 37-51 are rejected under 35 U.S.C. § 103(a) for allegedly being obvious over the combination of WO 2002/072113 ("Leek") in view of U.S. Publication 2004/0031067 ("Herlyn"), U.S. Patent 7,196,054 ("Drohan"), and U.S. Publication 2002/0018757 ("Harichian").

Applicant respectfully disagrees with the positions taken by the Examiner in the response. However, in an effort to further the prosecution and secure prompt allowance, claim 1 has been revised to state:

> A wound healing composition comprising living human dermal fibroblast cells suspended within a single layered sterile, non-pyrogenic, solid or semi-solid, support matrix, said support matrix comprising a protein concentration of 3 to 12 $mg.ml^{-1}$ and a cell density of said human dermal fibroblasts of 450 to 2500 cells per mm^2, said composition having been incubated for 16 to 24 h at about 37°C.

By comparison, Leek fails to disclose or suggest several of the elements in the above claim such as the single layered, sterile, non-pyrogenic, protein concentration, cell density, and incubation period and temperature limitations. Further, the secondary references of Herlyn, Drohan, and Harichian fail to supplement Leek's deficiencies.

For instance, Herlyn is cited for disclosing a wound healing composition that has a matrix with a monolayer of human dermal fibroblasts at paragraph [0039] (Office Action at page 4). However, Applicant respectfully notes that Herlyn actually concerns a multi-layered construct having different cellular layers. Paragraph [0044] is illustrative of this:

> The reconstruct is built in layers. At the bottom is a layer of endothelium cells from which the growth medium has been removed. The matrix is built on top of the endothelial layer, as follows. The first layer is added on top of the endothelial cell layer. The first layer is an acellular layer of collagen type I, such as that available from Organogenesis (Canton, Mass.), which is allowed to polymerize. When polymerized, a second layer comprising collagen type I and fibroblasts is poured on top of the first layer and allowed to polymerize. The second layer preferably also contains smooth muscle cells. When the second layer has hardened, a supporting growth medium is added on top of the second layer. An example of an acceptable medium is modified MCDB131 to which 1-5% fetal bovine serum added. 1% fetal bovine serum is preferred.

Therefore, the actual wound healing composition described in Herlyn is a multi-layered composition. The Examiner appears to be picking and choosing from select portions of Herlyn without actually considering the reference in its entirety. If considered in its entirety, the end result would be that Herlyn suggests a multi-layered cellular construct to be used for wound healing. The reasonable combination of Herlyn with Leek is the production of a multi-layered construct having Leek's fibroblast containing composition layered onto Herlyn's endothelium cellular layer, which results in a multi-layered construct of different cells.

With respect to Drohan, this reference is cited for disclosing a fibrin matrix delivery system for use as a wound healing composition (Office Action at page 4). The Abstract of Drohan explains that the composition can include a protease inhibitor, among other ingredients,

as noted by the Examiner. However, if consideration of Drohan were to stop with a brief review of its Abstract without actually considering the entire reference, then a full and objective understanding of what Drohan suggests in view of Leek would be compromised.

Drohan concerns a tissue sealant (TS) that can be used to seal a wound and reduce blood loss while also maintaining hemostasis (col. 19, lines 51-57). The TS can be a fibrin glue and can be supplemented with growth factors or drugs to aid in healing the wound (col. 1, lines 31-41). This reference also appears to suggest that if the composition is to be used on humans, then the components are preferably pathogen-inactivated *via* detergent/solvent, pasteurization, or ultrafiltration (col. 26, lines 33-46). This would suggest that if any cells (*e.g.*, living human dermal fibroblasts) were present in Drohan's composition, such cells would be inactivated or made to be non-living. In this sense, the teachings of Drohan, which relies on a non-living tissue sealant to bring about its objective, are sufficiently different from those in Leek, which relies on living cells to bring about its objective, to call into question whether there is indeed an apparent reason to combine their teachings. *See* MPEP 2143.01(II).

As for Harichian, this reference is cited for disclosing skin care compositions that function to simulate collagen syntheses by fibroblasts in the skin (Action at page 4). As noted by the Examiner, Harichian's composition includes the protease inhibitor aprotinin. However, a complete reading of Harichian suggests that its compositions are standard topical skin formulations that are used to treat wrinkles and the appearance of aged skin (Abstract and paragraphs [0001], [0010], and [0085]. Nothing in this reference suggests using living cells, much less human dermal fibroblasts, for treating wounds. Rather, Harichian relies on the presence of gum mastic to promote, *inter alia*, collagen production in skin cells to which the composition has been applied to (paragraphs [0070]-[0085]). Therefore, the combination of Leek, which concerns treating open wounds, with Harichian, which concerns treating symptoms

associated with aged skin, seems to be sufficiently different to call into question as to whether there is an apparent reason to combine their teachings.

Further, a common theme amongst all of the cited references is that they are all deficient in teaching or suggesting a composition that has "been incubated for 16 to 24 h at about 37°C." Applicant requests that the Examiner give weight to this limitation. *See* MPEP § 2113 (explaining that "[t]he structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product.").

Applicant's composition having been incubated for 16 to 24 hours at about 37°C enjoys structural differences when compared with the cited compositions. Applicant's specification at page 9, line 29, to page 10, line 5, and corresponding data confirm:

> The present inventors have found that under normal culture conditions, for example, a liquid culture of human dermal fibroblasts incubated in a standard culture medium at 37°C, development of a wound-healing phenotype may typically take 2 to 3 days. However, incubation of such fibroblasts in a suitable environment such as in a support matrix and/or a wound shortens the development process, so that before 24 hours the cells may have entered or reached the wound-healing phenotype. Thus, incubation of cells in a suitable support matrix and/or wound results in a shorter development time to reach a wound healing phenotype than standard (for example, liquid) culture conditions.

The specification also explains that this shorter development time to produce a wound-healing phenotype was surprising in that it results in a composition that is in an optimal stage "for accelerating or assisting wound healing" (page 8, lines 21-30) which includes the cells being "optimally suited for secretion of extraceullular matrix with minimal inappropriate fibrinnolysis" (page 10, line 31, to page 11, line 1).

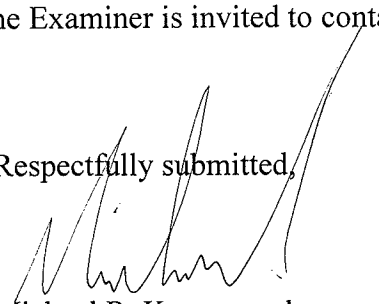
Given that the combination of Leek with Herlyn, Drohan, and Harichian fails to disclose or suggest Applicant's claimed composition "having been incubated for 16 to 24 h at about 37°C," it is respectfully submitted that the current obviousness rejection cannot be maintained.

For at least all of the reasons stated above, Applicant requests that the current obviousness rejection be withdrawn.

D. Conclusion

Applicant requests that this case proceed to allowance. Should their be any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-3020.

Respectfully submitted,



Michael R. Krawzsenek
Reg. No. 51,898
Attorney for Applicants

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 536-3020
(512) 536-4598 (facsimile)

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